

### REMARKS

Claims 10, 14, 15 and 36-38 remain pending in the application. Claims 1-9, 11-13 and 16-35 have been cancelled.

Applicants' paper filed on April 30, 2009 was not entered. Therefore, the claims are herein amended from their form as amended November 6, 2008.

Claims 10 and 36 are amended to recite that the p97 that is utilized in the claimed method is unconjugated to any moiety. Applicants submit that a person skilled in the art would acknowledge that it is quite clear throughout the specification that p97 is used in an unconjugated form. There is not a single instance in the specification where conjugation of p97 to any other moiety is described, and the protein is referred to consistently throughout the specification simply as "soluble p97". Also, many instances can be found describing addition of "p97 alone" to culture media or describing the effects of "p97 alone" in discussion of experimental results. See, e.g. page 45, lines 10-14, where it is described that, "While soluble p97 or plasminogen alone did not induce cell detachment, . . .". Such description recites in positive terms that the soluble p97 is not covalently attached to any further substance, that is, it is unconjugated to any further moiety.

#### Rejections for lack of novelty

Claims 32 and 36-38 stand rejected under 35 USC § 102(b) as being anticipated by Gabathuler. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

As has been previously explained, the rejection is made because the Examiner inappropriately interprets the claims as including p97 conjugated to some further substance. However, in the Advisory Action issued May 22, 2009, the Examiner also acknowledges that Gabathuler only teaches a composition including soluble p97. The Examiner specifically pointed out paragraph 27 as the key passage in Gabathuler which supposedly anticipates the present invention. In this regard, the claims have been amended to only be directed to a method

of treating cancer, which is nowhere taught or disclosed in Gabathuler. Claim 32, directed to a composition, has been cancelled. Further, Applicants completely disagree with the Examiner's interpretation of the case law that the transitional phrase "comprising" in the claims allows the modification of a specifically described element to include further aspects. While it is so that the transition "comprising" when used in a method claim allows for inclusion of additional steps it does not allow for inclusion of structures additional to those specifically recited for implementing a recited step. In this regard, Applicants note that most of the cases cited to support the Examiner's position relate to the use of the term "comprising" in claims to compositions or articles of manufacture, where indeed additional ingredients or further elements can be included by the term. The sole case cited relating to method claims, *Invitrogen Corp. v. Biocrest Mfg.*, as quoted by the Examiner, agrees with Applicants Representatives assertion; to wit, "The transition "comprising" in a method claim indicates that the claim is open-ended and allows for additional step" (emphasis added). ***The Examiner should note that there is nothing indicating that the case stands for the proposition that structures for carrying out any particularly recited step can be modified beyond what is described expressly in the claim.***

Nonetheless, so as to advance the prosecution of the application, the claims have been amended so as to make clear that the p97 utilized in the claimed method is not conjugated to any further moiety, and to no longer be directed to a composition. Therefore, the present claims are distinct from what is disclosed by Gabathuler and the so the instant rejection should be withdrawn.

Claims 10, 14, 15, 32 and 36-38 stand rejected under 35 USC § 102(e) as anticipated by Jefferies et al. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

Again, as has been previously explained and indeed acknowledged by the Examiner, the basis for this rejection is that the Examiner interprets the recitation of "comprising" as the transitional phrase to allow for modification of a specifically recited element of the claim to include further features. Further, in the Advisory Action issued May 22, 2009, the Examiner seems to indicate that Jefferies et al. contemplates the use of an unconjugated p97 (column 9

lines 5-7) and the use of p97 for the treatment of diseases including skin cancer (column 6 lines 55-60, column 7 line 65-column 8 line 8, column 8 lines 57-61).

So as to advance the prosecution of the application, the claims have been amended to make clear that the p97 utilized in the claimed method is not conjugated to any further moiety, and to no longer be directed to a composition. The claims are now only directed to a method of treating cancer using an unconjugated p97. Such a method is nowhere taught or disclosed in Jefferies.

Furthermore, a person skilled in the art would acknowledge that Jefferies is only teaching the use of conjugated p97 to modulate iron uptake in cells and indirectly to modulate iron metabolism using p97, which can be involved in treating some conditions involving disturbance of iron metabolism, such as tumors, and in particular skin cancer (see column 6 lines 55-60 and column 7 line 65-column 8 line 8). On the contrary, the present invention is not directed to the use of p97 to modulate iron uptake. In addition, enclosed herewith are a copy of the references of Richardson, Sekyere et al. (2005), Dunn et al., Rahmanto et al. and Sekyere et al. (2006) demonstrating that the hypothesis formulated by Jefferies is not viable. As clearly mentioned in the reference of Sekyere et al. (2005), MTf (p97) can bind Fe from Fe-citrate, but plays little role in Fe uptake by cells compared to Fe uptake from Tf (transferrin) by the transferrin receptor 1. In the reference of Dunn et al., it is clearly indicated that MTf has a negligible role in cellular Fe uptake in melanoma cells, as reaffirmed by Rahmanto et al. MTf<sup>-/-</sup> mice were viable and fertile and developed normally (see Sekyere et al., 2006). Assessment of Fe indices, tissue Fe levels, haematology and serum chemistry parameters demonstrated no differences between MTf<sup>-/-</sup> and wild-type mice, demonstrating that MTf is not essential for Fe metabolism. Therefore, it is now clear in light of these reference that the hypothesis that p97 can modulate iron uptake in cells and indirectly modulate iron metabolism which can be involved in treating some conditions involving disturbance of iron metabolism, is not based on scientific facts as demonstrated by the references submitted herewith. Thus, Jefferies et al. is not enabling for the use of p97 to treat any disease since it is only based on the supposed ability of p97 to modulate iron uptake which as now been demonstrated has being an inaccurate hypothesis.

A person skilled in the art would conclude that Jefferies teaches away from the present invention since the cited reference is only extrapolating the potential use of p97 to treat some diseases associated with a disturbance in iron metabolism, without presenting any evidence that p97 could be used to treat a disease by another mechanism or another pathway, as clearly demonstrated in the present application. Accordingly, the present claims are distinct from what is disclosed by Jefferies and the instant rejection should be withdrawn.


Applicants submit that the present application claims subject matter patentable over the prior art of record. The favorable actions of withdrawal of the standing rejections and allowance of the claims are requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Mark J. Nuell, Ph.D., Reg. No. 36,623 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

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Respectfully submitted,

By 

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